

Abstract

The present invention provides novel heterobifunctional and monobifunctional polyethylene glycol derivatives for the pegylation of therapeutically active proteins. The heterobifunctional PEGs which bear two different functional groups as well as the
5 monobifunctional PEGs which contain two similar functional groups, may be used for cross-linking purposes. The cross-linking may be intramolecular between two areas within the same molecule or intermolecular between two separate molecules. The pegylated protein conjugates that are produced, retain a substantial portion of their therapeutic activity and are less immunogenic than the protein from which the
10 conjugate is derived. New syntheses for preparing such bifunctional derivatives are described.